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Chapter

Future of Nanoparticles in the Field of Medicine

Neha Sharma

Abstract

The chapter deals with the application of iron oxide nanoparticles in the field of medicine. It focuses on the treatment of cancerous cells in the body as a case study. Cancer as we all know is a disease which is spreading at the speed of light across the nations, primarily due to the lifestyles and heredity. The human war against the disease is on, and many cures are in practice or under research, so as to limit the deaths due to it. Most of the research is focused on finding alternative and effective techniques in conquering cancer, so that the stigma attached with it can be diminished; the researchers are also focusing on lowering the side effects of the currently practiced cures. We all hope that a day will come when it will come under the category of conquerable diseases. It has been shown that cancer deaths in the world have declined considerably, but it is still unconquerable. It is still one of the leading causes of death around the globe. Usual therapy like radiation, surgery, and immunotherapy in addition to chemotherapy has shown challenges like ease of access to the tumor cells, danger of operating on a vital organ to name some. Off late, research laboratories are using nanoparticles for the detection in addition to drug delivery in treatment of various diseases. It gives boost to minimizing the side effects encountered in conventional therapies at the cellular and tissue level. Nanoparticles' widespread use is accounted by their size.

Keywords: magnetic nanoparticles, tumor, hyperthermia

1. Introduction

The discussion in the succeeding paragraphs is not limited to only iron oxide nanoparticles, it deals with all nanoparticles which are magnetic in nature; hence, there is a reoccurrence of the phrase "magnetic nanoparticles."

The technique or the procedure which I am going to discuss is widely known as hyperthermia. It is the phenomenon which involves selective heating of magnetic particles using high-frequency magnetic field. The case presented here uses the fact that the tumor in the affected area can be removed by heating it up to certain temperatures depending on the different parameters of the nanoparticles. The whole idea started with the introduction of the magic bullet, a concept given by Nobel laureate Paul Ehrlich (1854–1915), 1908, in the field of medicine in the field of immunity. The idea of Magic Bullet projected by selective targeting of disease causing organism in addition to delivery of toxin for the affected area. The procedure suggested was to first identify the cancerous cell/tissue and then target the magic bullet of nanoparticles at the site and the blast the cell for destroying the

un-repairable cell or delivering dose with the help of nanoparticles' magic bullet, which at the site will open to deliver the drug.

Later, after the invention of the magic bullet, a number of hyperthermia techniques were suggested since 1970. Scientists Zimmermann and Pilwat in 1976 proposed the use of magnetic erythrocytes for delivery of drug at the affected site. Research group led by Freeman et al. in 1960 came up with the idea wherein magnetic nanoparticles could be transported through the vascular system and grouped in a specific part of the body using magnetic field. As recently as 2009, Boris Polyak and Gary Friedman explored clinical potential and applications of magnetic targeting for site-specific drug delivery.

The treatment of hyperthermia involves heating of injected cancer-specific biomolecules coated with magnetic nanoparticles at the affected area. It involves selective heating of magnetic particles, which are positioned at the affected site, using high-frequency magnetic field. Removal of tumor (different diameter sizes) located in the liver is studied by varying power applied for different exposure times theoretically using heating model given by Tsafnat et al.

I again present the research by my group wherein we optimized the power requirements for the destruction of diseased cell at the location. The entire work was around the concept of the treatment of tumor using hyperthermia, which involves heating of injected cancer-specific biomolecules coated with magnetic nanoparticles at the affected area. The procedure involved selective heating of magnetic nanoparticles, which are positioned at the affected site of the diseased cell, using a very high-frequency magnetic field. The hypothesis used is that the tumor in the affected area can be removed by heating it up to temperatures, in the range of 41–46°C based on earlier research in the area. It was proposed that a tumor with a diameter size of 5 cm can be efficiently removed, if magnetic nanoparticles (present at the tumor site) were exposed for 10 s, with a power range of 2.75–6.5 W.

2. Approach

Based on the different research models given, we used the theory according to which the tumor in the affected area can be removed by heating it up to temperatures [1–19, 26], in the range of 41–46°C. It was proposed that if the power ranges 2.75–6.5 W, when applied to the magnetic nanoparticles (present at the tumor site), for duration of (up to) 10 s, a tumor having diameter of size 5 cm can be successfully/efficiently removed. Dependency of temperature in the affected area on the diameter of the magnetic nanoparticle in addition to exposure time of magnetic nanoparticles by alternating magnetic field and power was studied [25, 26].

The work tries to carry forward the results presented in orphan drugs [20], which proved that, if heat is applied for a duration of 10 s for an applied power to magnetic nanoparticles of 6.5 W, it leads to removal of tumor (up to radius size of 10 cm). We explore the variation in applied power within which the desired results can be obtained, which in turn leads to minimizing the running cost and undue heating of healthy tissue/cell in the vicinity of the affected area. The study presented is based on the model suggested by Tsafnat et al. [19] for heating of liver tumors. According to their study, the affected area demonstrates lower levels of blood perfusion than a healthy one. This results in partial safety for the healthy liver tissue during localized hyperthermia treatment. The model (mathematical) reproduced here simulates the practical heat diffusion from the affected area (tumor) to its surrounding (unaffected) tissue. It is assumed that temperatures in the two respective areas have an effect on each other at the boundary interface.

3. The mathematical model

It is assumed that the shape of the tumor is a spherical tissue with radius a which is surrounded by a normal tissue again assumed to be a bigger concentric sphere with radius b (see **Figure 1**).

The model presented also works on a hypothesis that the heat source with constant power density P is concentrated within the small sphere of radius a surrounded by a medium of homogenous heat conductivity.

As the model under study is having the spherical symmetry and the homogenous time-independent power density P inside the sphere, the temperature distribution is a function of distance r from the center of the sphere and on time t.

The differential equations of heat conduction [11, 20, 24] are used for defining the required mathematical model given by [11, 20, 24]

$$c_1\rho_1\frac{\partial T_1}{\partial t}=\frac{k_1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T_1}{\partial r}\right)+P,\ \text{for}\ 0\le r<a,\ \text{interior of tumor} \tag{1}$$

$$c_2\rho_2\frac{\partial T_2}{\partial t}=\frac{k_2}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial T_2}{\partial r}\right)\ \text{for}\ a\le r\le b,\ \text{exterior of tumor} \tag{2}$$

The subscript "1" is used to represent tumor tissue, while the subscript "2" refers to normal tissue, and the various parameters in these equations are defined as follows:

T is for the temperature.

c represents specific heat capacity.

ρ represents the density.

k is the heat conductivity.

Based on the hypothesis that the temperature and flux at the boundary are continuous and fine, the boundary conditions can be written as

$$T_1(a,t)=T_2(a,t) \tag{3}$$

$$k_1\frac{\partial T_1(a,t)}{\partial r}=k_2\frac{\partial T_2(a,t)}{\partial r} \tag{4}$$

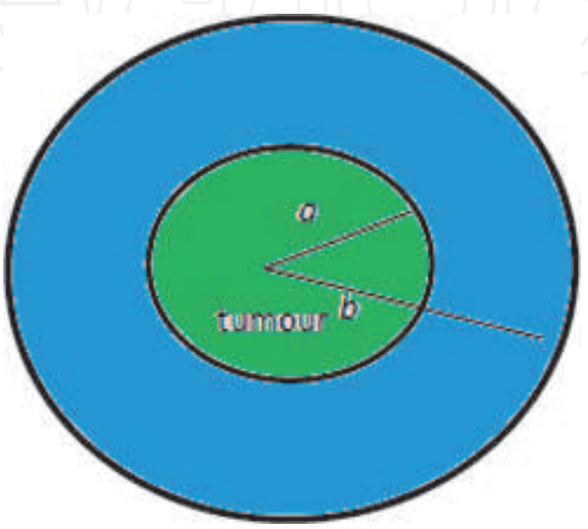

Figure 1.
Tumor tissue, spherical in shape, surrounded by normal tissue concentric sphere [26].

$$T_1(0,t)\ \text{isfinite} \tag{5}$$

$$T_1(r,0)=T_0 \tag{6}$$

$$T_2(r,0)=T_0 \tag{7}$$

To solve the above system of differential equations, we discretize it using the Euler method, which is reproduced here [26].

Let h > 0 and k > 0 be the step lengths in the space and time directions, respectively. Also let N1 and N2 be integers such that

$$\text{hN1} = \text{a and hN 2} = \text{b}. \tag{7a}$$

We replace the region Ω = {(r,t) l 0 ≤ r ≤ b, t ≥ 0} by a set of grid points (r_1, t_j), denoted by (l, j),

where

$$r_1 = \text{lh}, t_j = \text{jk}, j = 0, 1, 2, \ldots, J \text{ and } l = 0, 1, \ldots N_2. \tag{7b}$$

where J is a positive integer.

Let

$$(T_1)_l^j = T_1(r_l,t_j) \text{ and } (T_2)_l^j = T_2(r_l,t_j) \tag{7c}$$

denote the solution of (1) and (2), respectively, at the grid point (l, j).

We approximate the solution of (1), (2) at the grid point (l, j) by the scheme

$$(T_1)_l^{j+1}-(T_1)_l^j=\frac{k_1k}{c_1\rho_1h^2}\left[\left((T_1)_{l+1}^{j+1}-(T_1)_l^{j+1}\right)-\left(1-\frac{2k}{r}\right)\left((T_1)_l^{j+1}-(T_1)_{l-1}^{j+1}\right)\right]+\frac{Pk}{c_1\rho_1}, \tag{8}$$

$$0<l<N_1$$

$$(T_2)_l^{j+1}-(T_2)_l^j=\frac{k_2k}{c_2\rho_2h^2}\left[\left((T_2)_{l+1}^{j+1}-(T_2)_l^{j+1}\right)-\left(1-\frac{2k}{r}\right)\left((T_2)_l^{j+1}-(T_2)_{l-1}^{j+1}\right)\right]+\frac{Pk}{c_2\rho_2}, \tag{9}$$

$$N_1<l<N_2$$

$$(T_1)_0^{j+1}-(T_1)_0^j=\frac{k_1k}{c_1\rho_1h^2}\left((T_1)_1^j-(T_1)_0^j\right)+\frac{Pk}{c_1\rho_1}, \tag{10}$$

From the boundary condition at the tumor-healthy tissue edge, we can write the approximation at the grid point (N_1, j) as

Parameter	Constant	Value
Radius of liver tumor	A	2.50 cm
Tumorous liver tissue specific heat	c_1	3.758 kJ/kg K
Healthy liver tissue specific heat	c_2	3.617 kJ/kg K
Liver tissue heat conductance	k_1=k_2	0.5122 W/m K
Liver density	$\rho_1 = \rho_2$	1.0492 g/mL

Table 1.
Liver tissue and nanoparticle parameters [11, 21–23].

$$(T_1)^j_{N_1} = (T_2)^j_{N_1} = \frac{k_1 (T_1)^J_{N_1-1} + k_2 (T_2)^J_{N_1}}{k_1 + k_2} \tag{11}$$

Solving Eqs. (8)–(11), using values of the different constants from **Table 1** [11, 21–23], the graphs can be plotted for studying dependency of temperature in and around tumor on radius (of tumor), time (of heat exposure), and power applied (on magnetic nanoparticles).

4. Results and discussion

From **Table 1**, it can be observed that varying r from center (0 cm) to the boundary of the affected area (=a), time of exposure up to 10 s with power ranging

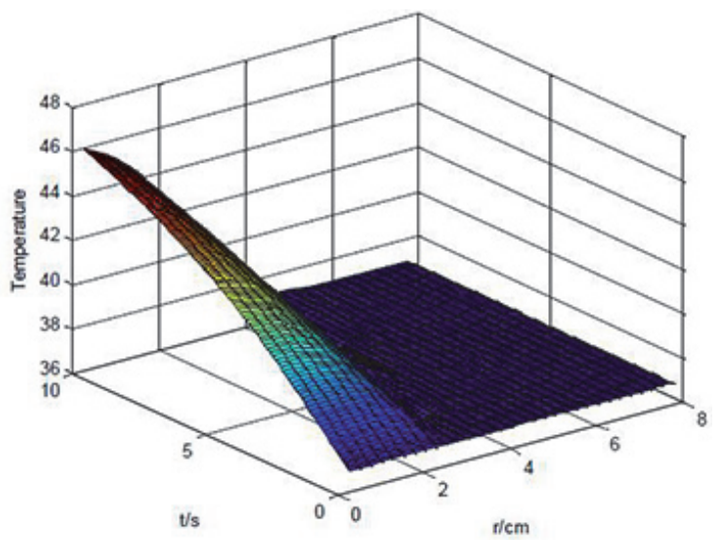

Figure 2.
For a constant magnetic nanoparticle power of 5 W, temperature in the tumorous cell/tissue plotted, as a surface plot and as a function of hyperthermia time (t, in s) and distance from the center of the tumor (r, in cm) [26].

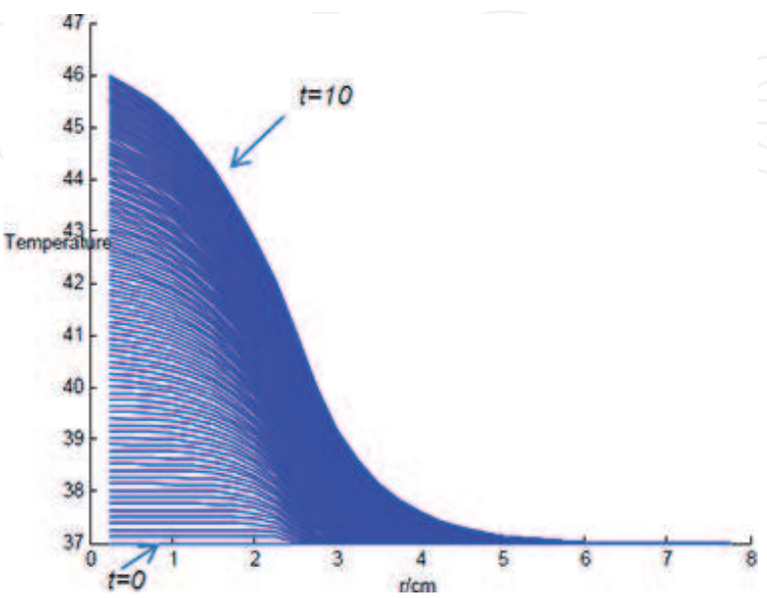

Figure 3.
For a constant magnetic nanoparticle power of 5 W, plot of temperature inside the tumorous cell/tissue as a function of distance from the center of the tumor (r in cm) and hyperthermia time (t, in s) [26].

from 2.75 to 6.5 W, MATLAB software is used to obtain **Figures 2–6**. In the given model, it was assumed that magnetic nanoparticles used were of the size up to 10 nm in radius. The surface plot (**Figure 2**) shows dependency of temperature in the affected area on hyperthermia time (t in s) and radius of the tumor (r in cm). It can be concluded from it that on application of 5 W power, temperature in tumor increases to 46°C at the middle region of the tumor, gradually reducing to body temperature at the interface (of affected and healthy area), thus causing least effect to the unaffected area. Similar conclusion can be drawn from **Figure 3**. The temperature variation at the center of the tumor on varying power of magnetic nanoparticles and time of heat exposure can be studied from **Figures 4** and **5**. It is observed that the temperature at the middle of the tumor cell gradually increases from body temperature at the interface (r=a) to 48°C for an applied power range of 2.75–6.5 W. It can be further observed that for a standard time of exposure (t = 7 s), if the power is varied from 2.75 to 6.5 W over a radius of 2.5 cm, it leads to annihilation of the tumor, from **Figure 6**.

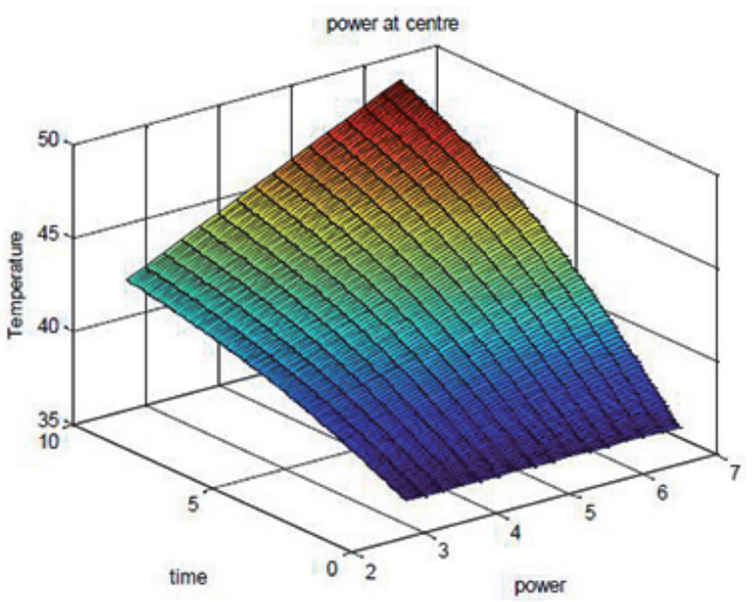

Figure 4.
Temperature at the center of the tumorous cell/tissue as a function of hyperthermia time (t in s) and a magnetic nanoparticle power (p, in Wts) [26].

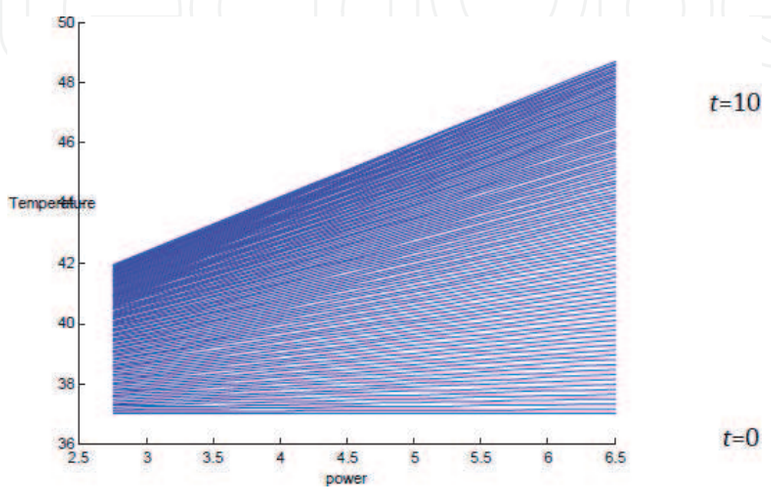

Figure 5.
Temperature at the center of the tumorous cell/tissue plotted as a function of magnetic nanoparticle power (p, in W) and hyperthermia time (t, in s) [26].

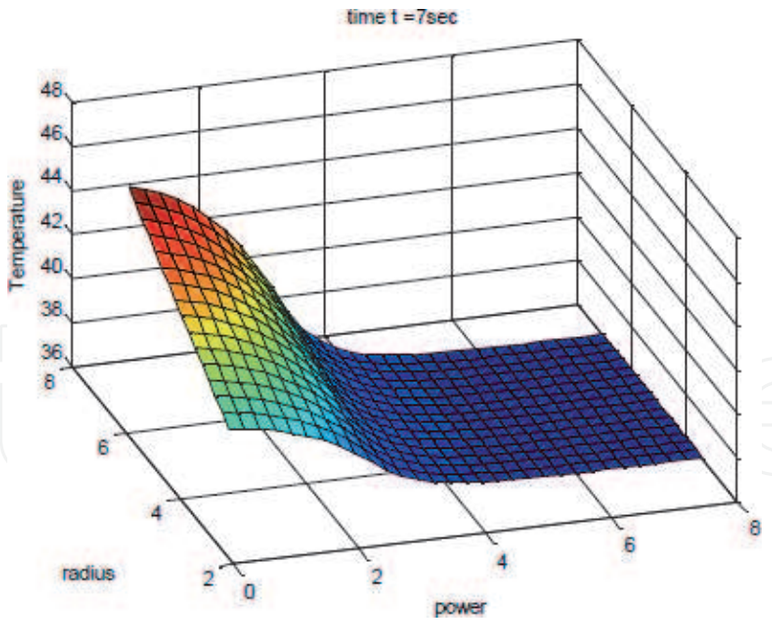

Figure 6.
Temperature in the tumorous cell/tissue plotted as a function of distance from the center of the tumor (r, in cm) and magnetic nanoparticle power (p, in watts) for a constant exposure time (t = 7 s) [26].

5. Conclusion

From the discussion, it can be concluded that hyperthermia treatment involving magnetic nanoparticles can be efficiently and effectively used for the removal of tumorous cell/tissue with not much collateral damage. Reduced damage to the neighboring healthy cells makes the technique more successful, clinical results are also in tandem with results if we use nanoparticles with power in the range of 2.75–6.5 W with a heat exposure time up to 10 s, this futuristic approach will make treatment more effective with fewer side effects and less cost, leading to widespread use and finally conquering the disease, which even in this robotic age is considered a taboo.

As recently engineers from MIT are working on designing of tiny robots, in nano range, which can assist in drug delivery, the engineered robots called the "microbots" are based on bacterial propulsion. The scientists have proposed that the procedure can help in overcoming the hindrances to drug delivery loaded with nanoparticles, enabling them to exit blood vessels and hit the right place [27].

As recently as March 2019, Angl Apostolov et al. reported the study based on similar concept of destroying hyperthermia. The group suggests, theoretically, the use of mixed ferrite nanoparticles with structure formula $Me_{1-x}Zn_xFe_2O_4$ (Me = Co, Ni, Cu, Mn) appropriated for self-controlled magnetic hyperthermia (SMHT) for both in vivo and in vitro applications.

Thus, there is a lot of scope in the area which can be reinvented and researched to make the world if not free at least less cancer deaths or sufferings.

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